

Drug Therapies for Insomnia

Payal Patel, Pharm.D. Candidate, Pinali Patel, Pharm.D, Megha Shah, Pharm.D. Candidate

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The New Jersey Drug Utilization Review Board assists the Division of Medical Assistance and Health Services and the Department of Health in the development of criteria and standards to be used in retrospective and prospective drug utilization review, to improve quality of care and reduce unnecessary expenditure. This guide contains information obtained from manufacturer's product package inserts, and is intended to provide healthcare professionals with a review of some of the uses and recommended dosing for the available sedative hypnotics. This information is intended ultimately to help control the pharmacy program prescription costs without affecting the health and welfare of the patients who are prescribed these pharmacological classes of medications.

Insomnia is the complaint of inadequate sleep. Need for sleep is variable, and treatment is needed only if it causes distress or daytime sleepiness. Insomnia may be caused by an underlying chronic health condition such as sleep apnea, unmanaged pain, or psychiatric illnesses and treating these may resolve the problem. Treatment may consist of a simple educational intervention regarding sleep hygiene in the form of patient handouts or counseling offered by a healthcare professional. Insomnia that persists may require the use of medications, preferably for a short period since long-term usage may lead to dependence and the inability to sleep independently. Sedative-hypnotic medications are most frequently prescribed to treat problems associated with falling asleep, duration and/or quality of sleep. The patient assessment must include drug and alcohol abuse potential since there is cross addiction and additive effects when using these medications. Within recent years, a new class of hypnotic agents referred to as the "Z" drugs have dominated the sleep market. The marketing emphasis for these new agents is based on their structural and binding site differences when compared to the benzodiazepines (BDZ). However they carry the same schedule IV classification and work by the same mechanism of action as the older BDZ. These newer agents may have less potential for rebound insomnia and withdrawal symptoms however they still have a potential for abuse. A single new "Non-Z" agent which is a melatonin receptor agonist is not classified as a scheduled drug and is approved for long term use. The initial BDZ drugs were studied and marketed as anti-anxiety agents and not hypnotics. All BDZ agents exhibit GABA-ergic agonist properties, are clinically studied and used to treat anxiety, but are often prescribed off-label as hypnotics. Gradually, a number of BDZ were marketed and released as solely hypnotic agents. The accompanying chart compares certain pharmacokinetic features of the various new and some older agents, as well as the cost categories based on fee-for-service Medicaid clients.

Non-Pharmacological Treatment

Sleep Hygiene Recommendations	<ul style="list-style-type: none">-Avoid daytime napping-No caffeine intake after 3:00 pm-Avoid large meals at night-Increase daily exercise (not immediately before bedtime)-Avoid stimulating activities before bedtime (action movies or computer games; instead read a book or meditate)-If unable to sleep in 30 minutes, leave bedroom and return when sleepy-If worries or plans are keeping you awake, leave bedroom and write plans, then return to bed	
Behavioral Therapies	<ul style="list-style-type: none">-Bright Light Therapy-Relaxation Techniques	<ul style="list-style-type: none">-Sleep Restriction-Stimulus Control Therapy

These treatments are not associated with abuse potential, drug dependence, or unwanted side effects. Sleep hygiene can easily be taught through educational materials or brief counseling at a medical visit. The behavioral therapies listed should be administered by a trained therapist.

What are the advantages of using sedative hypnotics for short-term treatment periods?

Prescribing short-term usage of sedative hypnotics prevents the following side effects of long-term treatment and also decreases the risk of rebound insomnia:

- ↑ in morbidity
- Tolerance
- Withdrawal Effects
- Addiction
- Respiratory depression
- Minimize risk of side effects

Rationale for Pharmacotherapy Use:

- Use lowest effective dose
- Use intermittent dosing (twice weekly to four times weekly)
- Prescribe medication for short term use (no more than 3-4 weeks)
- Discontinue medication gradually
- Be alert for rebound insomnia following discontinuation
- Use agents with shorter elimination half-life to reduce day time sedation
- Greater risk for sedative effects with renal or hepatic insufficiency

Questions to ask patients while monitoring hypnotic therapy:

- Is your sleep improving? (ability to fall asleep, stay asleep, not waking up early)
- Are you taking the medication as prescribed?
- Are you experiencing sleepiness in the morning or during the day?
- Have you noticed changes in your mood, behavior, or memory?
- Are you more nervous, irritable, or anxious than usual?
- Are you having problems with dizziness, lightheadedness, or unsteadiness?

Drug Name	Class/Schedule/ Relative Cost	Indication	Dosage & Administration	t _{1/2} (hr)	Onset of Action (min)	Duration of Action (hr)
alprazolam (Xanax [®])	GABA-BDZ receptor agonist C-IV \$	No FDA indication for tx of insomnia	0.25, 0.5, 1, 2 mg Adults or Elderly: No dosing for insomnia available	6.3-26.9 (11.2)	Intermediate	No data
estazolam (Prosom [®])	GABA-BDZ receptor agonist C-IV \$	Short-term tx of insomnia	1, 2 mg -Adults: 1 mg at bedtime -Small, Debilitated or Elderly: 0.5 mg	8-28 No active metabolite	No data	No data
eszopiclone (Lunesta [®])	GABA-BDZ receptor agonist C-IV \$\$\$	Long-term tx of insomnia (no result in 7-10 days patient should be re-evaluated)	1, 2, 3 mg -Adults: 2 mg before bedtime -Hepatic Impairment or Elderly: 1mg before bedtime	5-7	30	1-3
flurazepam (Dalmane [®])	GABA-BDZ receptor agonist C-IV \$	Short-term tx of insomnia (28 days)	15, 30 mg -Adults: 30 mg before bedtime -Elderly or Debilitated: 15 mg before bedtime	2-3 Active metabolite: (47-100)	17	7-8
lorazepam (Ativan [®])	GABA-BDZ receptor agonist C-IV \$	Unlabeled use: Short-term improvement of chronic insomnia	2 or 4 mg at bedtime for insomnia due to anxiety or transient stress	10-20	Intermediate	No data
quazepam (Doral [®])	GABA-BDZ receptor agonist C-IV \$	Short-term tx of insomnia (28 days)	7.5, 15 mg -Adults: 15 mg at bedtime, maybe ↓ to 7.5 mg -Elderly: 7.5 mg at bedtime, if not effective in 1 to 2 nights ↑ dose to 15 mg	25-41 Active metabolite: (47-100)	No data	No data
ramelteon (Rozerem [®])	Melatonin receptor agonist Non-controlled \$\$\$	Long-term tx of insomnia characterized by difficulty with sleep onset	8 mg -One-half hour before bedtime -Mild to Moderate Hepatic Impairment: use with caution -Severe Hepatic Impairment: Use not recommended	1-3	30	*Studied for sleep onset
temazepam (Restoril [®])	GABA-BDZ receptor agonist C-IV \$	Short-term tx of insomnia (7-10 days)	7.5, 15, 30 mg -Adults: 15-30 mg at bedtime -Elderly: 15 mg at bedtime	3.5-18.4 No active metabolite	30-60	8-10
triazolam (Halcion [®])	GABA-BDZ receptor agonist C-IV \$	Short-term tx of insomnia (28 days)	0.125, 0.5 mg -Adults: 0.25 mg before bedtime (**maximum dose 0.5 mg**) -Elderly or Debilitated: 0.125 mg to 0.25 mg before bedtime (**maximum dose 0.25 mg**)	1.5-5.5 No active metabolite	No data	No data
zaleplon (Sonata [®])	GABA-BDZ receptor agonist C-IV \$\$\$	Short-term tx of insomnia (< 7-10 days)	5, 10 mg -Adults: 10 mg before bedtime -Elderly: 5 mg before bedtime -Mild to Moderate Hepatic Impairment: 5mg before bedtime -Severe Hepatic Impairment: Use not recommended	~1	Rapid	6-8
zolpidem tartarate (Ambien [®]) zolpidem tartarate ER (Ambien CR [®])	GABA-BDZ receptor agonist C-IV \$\$\$	Short-term tx of insomnia (7-14 days)	5, 10 mg -Adults: 10 mg at bedtime -Hepatic Impairment: 5 mg at bedtime 6.25, 12.5 mg -Adults: 12.5 mg at bedtime -Hepatic Impairment: 6.25 mg at bedtime	2-2.6	30	6-8

- Footnotes:
1. Take extreme caution while driving or operating heavy machinery while on these medications.
 2. All of these medications need to be taken on an empty stomach and should not be taken with alcohol, CNS depressants,azole anti-fungals, or SSRI's. High fatty meals will impede the absorption of these drugs.
 3. Consult full prescribing information for pharmacokinetics of individual agents.
 4. \$\$\$ (most expensive per pill)-\$ (least expensive per pill)

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